Translation

PCT Application
PCT/JP2003/000261

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT03001	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/000261	International filing date (*day/month/year*) 15 January 2003 (15.01.2003)	Priority date (*day/month/year*) 15 January 2002 (15.01.2002)
International Patent Classification (IPC) or national classification and IPC C12Q 1/68, C12N 15/09, G01N 33/50		
Applicant GENESYS TECHNOLOGIES, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 10 March 2003 (10.03.2003)	Date of completion of this report 17 December 2003 (17.12.2003)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

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International Application No.
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I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-23, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:

pages 2-3, 5-8, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages (1, 4, 11-15), (11-15), filed with the letter of (05.09.03), (09.06.03)

☒ the drawings:

pages 1/8-8/8, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☒ the claims, Nos. 9-10
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 15

because:

☒ the said international application, or the said claims Nos. 15 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See supplemental sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III. 1.

Claim 15 relates simply to "computer programs" not defined by specific means combining software and hardware resources.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8, 11-14	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-8, 11-14	NO
Industrial applicability (IA)	Claims	1-8, 11-14	YES
	Claims		NO

2. Citations and explanations

Document 1: ~~Toshiraki~~ Itsuro Inoue, "Idenshi tagata o riyou shita shikkan idenshi kensakuhou, 'post sequence' no 'genome' kagaku (1) SNP idenshi tagata no senryaku", first edition, Nakayama-Shoten Co., Ltd., 2000, pp. 47-70

Document 2: American Journal of Human Genetics, 2000, Vol. 66, No. 6, pp. 1833-1844

Claims 1-8 and 11-14

The inventions set forth in claims 1-8 and 11-14 do not involve an inventive step in the light of document 1 cited in the international search report.

Document 1 discloses a method for identifying disease-related SNPs by means of haplotype analysis, etc. It also discloses testing of typing data by methods such as testing Hardy-Weinberg equilibrium and the χ^2 test when employing said method.

In this connection, screening of chromosomes for gene loci linked with diseases and narrowing them down by stages is common within the art, as also disclosed in document 1. Therefore, no special difficulty is entailed in narrowing down by stages from a region of a chromosome to an SNP of interest in the method for identifying SNPs disclosed in document 1. In addition, document 2 discloses

haplotype analysis with scanning of small regions referred to as windows. In this connection, in the written reply dated 5 December 2003, the applicant asserts that the approach to analysis described in the present patent considers primarily the situation in which it is impossible to predict regions of relevant genes beforehand and that it is a process model for an approach focussing on efficient specification of haplotype blocks which include polymorphs of a relevant gene in such a situation, whereas document 2 requires data such as genealogical tables and differs from the procedure used in the present inventions. However, in itself scanning of small regions
x termed windows is recognized to be a procedure commonly used within the art when performing haplotype analysis, irrespective of whether or not it is possible to predict regions of relevant genes beforehand and, therefore, no
λ special difficulty is entailed in (also) scanning small regions termed windows when performing haplotype analysis in document 1.

Moreover, adoption of the constitution of the inventions described in claims 1-8 and 11-14 does not appear to offer any specially marked effects.

Revised Claims : Amendments under Article 34 (September 5, 2003)

1. (Revised) A method of specifying SNP related to disease susceptibility or drug responsiveness and comprising:

a first step of defining a continuous domain that contains a specified number of SNPs determined by a range of several to several tens as a window, and setting a scanning domain beforehand in said window that will be the object of SNP analysis;

a second step of gradually narrowing down said scanning domain to a localized domain that contains a target SNP; and

a third step of specifying said target SNP from said narrowed down localized domain.

Amended on Sep. 5, 2003

2. The method of specifying SNP of claim 1 wherein said second step comprises a step of setting a marker SNP for specifying said target SNP and gradually narrowing down said scanning domain.

3. The method of specifying SNP of the second claim wherein said second step uses statistical analysis such as haplotype analysis to set said marker SNP.

4. (Revised) The method of specifying SNP of claim 3 wherein

said first step comprises: a step of setting the scanning domain of said window in a genome domain that is limited to genes whose functions are clearly known or chromosomes whose functions can be predicted; and

said second step comprises:

a fourth step of selecting a group of SNP to be typed from said scanning domain and performing SNP typing using a wet process;

a fifth step of finding the probability of appearance of all combinations of said haplotype analysis in said scanning domain based on typing data of said SNP typing as a statistical amount; and

a sixth step of comparing the found said statistical amount with a

Amended on Sep. 5, 2003

Amended on 5. 2003 Sep. (continuation of Claim 4)

preset or estimated reference statistical amount, and when there is significant deviation between said statistical amount and said reference statistical amount that exceeds a preset threshold, determining that said marker SNP is contained in the domain corresponding to the deviated position that exceeds said threshold value.

5. The method of specifying SNP of claim 4 wherein said third step comprises:

a seventh step of increasing the specified ratio of the number of SNPs to be the object of typing in the selection of the SNP group in said fourth step when said significant deviation is less than a first threshold value, and then repeating said fifth step;

an eighth step of setting a new scanning domain from said scanning domain that has been decreased by a specified ratio such that it contains the position of the deviated peak when said significant deviation is greater than said first threshold value but less than a second threshold value, and then repeating said fifth step; and

a ninth step of determining that said marker SNP is contained in the domain corresponding to the deviated position that exceeds said second threshold value when said significant deviation exceeds said second threshold value, setting a new scanning domain from said scanning domain that has been decreased by a specified ratio such that it contains the position of the deviated peak, and then repeating said fifth step.

6. The method of specifying SNP of claim 5 wherein said ninth step comprises a step of setting SNPs that include the target SNP for which all DNA samples are typed when the number of SNPs in a selected group is less then a specified number.

7. The method of specifying SNP of claim 5 wherein said seventh step comprises a step of determining that the target SNP is not contained and stopping the process when the number of times the process of said fifth

step is performed exceeds a specified number of times.

8. The method of specifying SNP of claim 5 in which said eighth step comprises a step of determining that the target SNP is not contained and stopping the process when the number of times the process of said fifth step is performed exceeds a specified number of times.

9.

10.

11. The method of specifying SNP of any one of the claims 1 thru 8 that defines a continuous domain that contains a specified number of SNPs determined by a range of several to several tens as a window, and statistically finds the probability of appearance of each combination of haplotypes from SNP typing data (all samples) in said window.

Filed on Jun. 9, 2003 as PCT 34 Amendment

12. The method of specifying SNP of any one of the claims 1 thru 8 wherein the number of said SNP is ten.

13. The method of specifying SNP of any one of the claims 1 thru 8 wherein the number of said SNP is three to five.

14. The method of specifying SNP of any one of the claims 1 thru 13 that moves said window from the start to the end of the 'scanning domain' during the processing cycle, and analyzes the SNP data contained in said window.

15. A computer program that can be read by a computer that can execute the processing of the method of specifying SNP of any one of the claims 1 thru 14 wherein all of the steps of any one of the claims 1 thru 14 are coded.